10/566322

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/23391

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : A61K 39/00, 39/29; C07H 21/00
US CL : 530/350, 424/184.1, 189.1, 192.1; 536/23.1, 23.4, 23.72
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 530/350, 424/184.1, 189.1, 192.1; 536/23.1, 23.4, 23.72

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WEST, PubMed

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2003/0054337 A1 (BIRKETT, Ashley), 20 March 2003 (20.03.2003).	1-4, 103-106
A	PUMPENS et al., Hepatitis B Virus Core Particles as Epitope Carriers, Intervirology, Volume 38, pages 63-74 (1995).	1-4, 103-106
A	Zheng et al., The structure of hepadnaviral core antigens. Identification of free thiols and determination of the disulfide bonding pattern, Journal of Biological Chemistry, Volume 267 No. 13, pages 9422-9429 (May 1992).	1-4, 103-106

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"B" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
06 September 2005 (06.09.2005)	18 NOV 2005
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Zachariah Lucas Telephone No. 571-272-1600

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/23391

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-57 and 103-106 (in part), drawn to a composition comprising a heterologous antigens linked to one or more non-primate hepadnavirus core antigen sequences that comprises a loop region.

Group II, claim(s) 58-100 and 103-106 (in part), drawn to a composition comprising a heterologous antigens linked to one or more primate hepadnavirus core antigen sequences that comprises a loop region.

Group III, claim(s) 101 and 103-106 (in part), drawn to a composition comprising one or more non-primate hepadnavirus core antigen sequences that comprises a loop region wherein the C-terminal sequence of the hepadnavirus core antigen is replaced by from 1 to 100 amino acids.

Group IV, claim(s) 102 and 103-106 (in part), drawn to a composition comprising one or more primate hepadnavirus core antigen sequences that comprises a loop region wherein the C-terminal sequence of the hepadnavirus core antigen is replaced by from 1 to 100 amino acids.

Group V, claim(s) 107-140, drawn to a method for modifying non-primate hepadnavirus core antigen including replacing the C-terminal sequence.

Group VI, claim(s) 141-463, drawn to a method for modifying primate hepadnavirus core antigen including replacing the C-terminal sequence.

Group VII, claim(s) 164-169, drawn to a method for producing an immunogenic composition comprising a non-primate hepadnavirus core antigen, including modifying the heterologous antigen. .

Group VIII, claim(s) 170-175, drawn to a method for producing an immune response using a non-primate hepadnavirus core protein linked to a heterologous antigen and/or the vector encoding the aforementioned core protein-heterologous antigen polypeptide.

Group IX, claim(s) 176-181, drawn to a method for producing an immune response using a primate hepadnavirus core protein linked to a heterologous antigen where the C-terminal sequence of the core antigen is replaced by 1-100 amino acids devoid of Cys or the wt sequence and/or the vector encoding the aforementioned core protein-heterologous antigen polypeptide.

Group X, claim(s) 182-183, drawn to a method for producing an immunogenic compositions comprising a primate hepadnavirus core antigen, including modifying the heterologous antigen.

Further groupings

Subgroups of Group I:

*Note that Subgroups are further broken into subgroups as the technical feature of these subgroups does not make a contribution over the prior art, as outlined above, and therefore does not constitute a "special technical feature" or due to the numerous sequences.

Group I-A, claim(s) 1, 2-4, and 103-106 (in part)
Group I-B, claim(s) 1, 5, and 103-106 (in part)
Group I-C, claim(s) 1, 6, and 103-106 (in part)
Group I-D, claim(s) 1, 7, and 103-106 (in part)
Group I-E, claim(s) 1, 8, and 103-106 (in part)
Group I-F, claim(s) 1, 9-11, and 103-106 (in part)
Group I-f-1 through I-f-18 correspond to SEQ ID NOs: 239-256, respectively.
Group I-G, claim(s) 1,12, and 103-106 (in part)
Group I-H, claim(s) 1, 13, and 103-106 (in part)
Group I-I, claim(s) 1, 14, 15, 19-33, and 103-106 (in part)
Subgroups of I-I
Group I-I-1, claim(s) 1, 15, and 103-106 (in part)
Group I-I-2, claim(s) 1, 19-21, and 103-106 (in part)
Group I-I-3, claim(s) 1, 22, and 103-106 (in part)
Group I-I-4, claim(s) 1, 23-27, and 103-106 (in part)
Group I-I-4.1 through I-I-4.106 correspond to the terminal sequences R, C, K, A, RRC, and SEQ ID NOs: 2-20, 22-36, 42-56, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, and 183-228, respectively.
Group I-I-5, claim(s) 1, 28, and 103-106 (in part)
Group I-I-6, claim(s) 1, 29, and 103-106 (in part)
Group I-I-7, claim(s) 1, 30, and 103-106 (in part)
Group I-I-8, claim(s) 1, 31, and 103-106 (in part)
Group I-I-9, claim(s) 1, 32, and 103-106 (in part)
Group I-I-10, claim(s) 1, 33, and 103-106 (in part)
Group I- J, claim(s) 1,16-18, and 103-106 (in part)
Group I-K, claim(s) 1, 34-55, and 103-106 (in part)
Group I-K-1, claim(s) 1, 35, and 103-106 (in part)
Group I-K-2, claim(s) 1, 36-37, and 103-106 (in part)
Group I-K-3, claim(s) 1, 38-40, and 103-106 (in part)
Group I-K-4, claim(s) 1, 41, and 103-106 (in part)
Group I-K-5, claim(s) 1, 42, and 103-106 (in part)
Group I-K-6, claim(s) 1, 43-48, and 103-106 (in part)
Groups I-K-6.1 through I-K-6.106 correspond to the terminal sequences R, C, K, A, RRC, and SEQ ID NOs: 2-20, 22-36, 42-56, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, and 183-228, respectively.
Group I-K-7, claim(s) 1, 49, and 103-106 (in part)
Group I-K-8, claim(s) 1, 50, and 103-106 (in part)
Group I-K-9, claim(s) 1, 51, and 103-106 (in part)
Group I-K-10, claim(s) 1, 52, and 103-106 (in part)
Group I-K-11, claim(s) 1, 53, and 103-106 (in part)
Group I-K-12, claim(s) 1, 54, and 103-106 (in part)
Group I-K-13, claim(s) 1, 55-57, and 103-106 (in part)

Subgroups of Group II

**Note that Subgroups are further broken into subgroups as the technical feature of these subgroups does not make a contribution over the prior art, as outlined above, and therefore does not constitute a "special technical feature" or due to the numerous sequences.

Group II-A, claim(s) 58, 59, and 103-106 (in part)
Groups II-A-1.1 through II-A-1.106 correspond to the terminal sequences R, C, K, A, RRC, and SEQ ID NOs: 2-20, 22-36, 42-56, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, and 183-228, respectively.
Group II-B, claim(s) 58, 60-62, and 103-106 (in part)
Group II-C, claim(s) 58, 63, and 103-106 (in part)
Group II-D, claim(s) 58, 64, and 103-106 (in part)
Group II-E, claim(s) 58, 65, and 103-106 (in part)
Group II-F, claim(s) 58, 66, and 103-106 (in part)
Group II-G, claim(s) 58, 67, and 103-106 (in part)
Group II-H, claim(s) 58, 68, and 103-106 (in part)
Group II-I, claim(s) 58, 69-77, and 103-106 (in part)

Group II-I-1, claim(s) 58, 70, and 103-106 (in part)
Groups II-I-1.1 through II-I-1.7 correspond to SEQ ID NOs: 41 and 109-114, respectively.
Group II-I-2, claim(s) 58, 71-73, and 103-106 (in part)
Group II-I-3, claim(s) 58, 74-76, and 103-106 (in part)
Group II-I-4, claim(s) 58, 77, and 103-106 (in part)
Group II-J, claim(s) 58, 78, and 103-106 (in part)
Group II-K, claim(s) 58, 79, and 103-106 (in part)
Group II-L, claim(s) 58, 80, and 103-106 (in part)
Group II-M, claim(s) 58, 81, and 103-106 (in part)
Group II-N, claim(s) 58, 82, and 103-106 (in part)
Group II-O, claim(s) 58, 83, and 103-106 (in part)
Group II-P, claim(s) 58, 84-100, and 103-106 (in part)
Group II-P-1, claim(s) 58, 85, and 103-106 (in part)
Group II-P-2, claim(s) 58, 86-88, and 103-106 (in part)
Group II-P-3, claim(s) 58, 89-91, and 103-106 (in part)
Group II-P-4, claim(s) 58, 92, and 103-106 (in part)
Group II-P-5, claim(s) 58, 93-94, and 103-106 (in part)
Groups II-P-5.1 through II-P-5.106 correspond to the terminal sequences R, C, K, A, RRC, and SEQ ID NOs: 2-20, 22-36, 42-56, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, and 183-228, respectively.
Group II-P-6, claim(s) 58, 95, and 103-106 (in part)
Group II-P-7, claim(s) 58, 96, and 103-106 (in part)
Group II-P-8, claim(s) 58, 97, and 103-106 (in part)
Group II-P-9, claim(s) 58, 98, and 103-106 (in part)
Group II-P-10, claim(s) 58, 99, and 103-106 (in part)
Group II-P-11, claim(s) 58, 100, and 103-106 (in part)

Subgroups of Group V

***Note that Subgroups are further broken into subgroups as the technical feature of these subgroups does not make a contribution over the prior art, as outlined above, and therefore does not constitute a "special technical feature" or due to the numerous sequences.

Group V-A, claim(s) 107, 108
Group V-B, claim(s) 107, 109-110
Group V-C, claim(s) 107, 111-118
Groups V-C-1.1 to V-C-1.6 correspond to the sequences of SEQ ID NOs: 1 and 103-107 respectively.
Group V-D, claim(s) 107, 119-140
Group V-D-1, claim(s) 107, 120 (in part), and 121-122
Group V-D-2, claim(s) 107, 120 (in part), and 123-124
Group V-D-3, claim(s) 107, 120 (in part), and 125-126
Groups V-D-3.1 through V-D-3.6 correspond to the sequences of SEQ ID NOs: 119-124, respectively.
Group V-D-4, claim(s) 107, 120 (in part), and 127-128
Group V-D-5, claim(s) 107, 120 (in part), and 129-130
Group V-D-6, claim(s) 107, and 131
Group V-D-7, claim(s) 107, and 132
Group V-D-8, claim(s) 107, and 133
Group V-D-9, claim(s) 107, and 134-135
Groups V-D-9.1 through V-D-9.13 correspond to the sequences of SEQ ID NOs: 73-75, 77-81, 83, and 98-101, respectively.
Group V-D-10, claim(s) 107, and 136
Group V-D-11, claim(s) 107, and 137
Groups V-D-11.1 through V-D-11.23 correspond to the sequences of SEQ ID NOs: 70-92, respectively.
Group V-D-12, claim(s) 107, and 138-140

Subgroups of Group VI:

Group VI-A, claim(s) 141-142
Group VI-B, claim(s) 141, 143-144
Group VI-C, claim(s) 141, 145-147
Groups VI-C-1.1 to VI-C-1.7 correspond to the sequences of SEQ ID NOs: 41 and 109-114 respectively.
Group VI-D, claim(s) 141, 148-157
Group VI-D-1, claim(s) 141, 148-151
Group VI-D-2, claim(s) 141, 148-149, 152-157

Group VI-E, claim(s) 141, 158
Group VI-F, claim(s) 141, 159
Group VI-G, claim(s) 141, 160-161
Groups VI-G-1.1 through VI-G-1.13 correspond to the sequences of SEQ ID NOs: 73-75, 77-81, 83, and 98-101, respectively.
Group VI-H, claim(s) 141, 162
Group VI-I, claim(s) 141, 163
Groups VI-I-1.1 through VI-I-1.23 correspond to the sequences of SEQ ID NOs: 70-92, respectively.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

The species correspond to the various SEQ ID NOs found in the claims. For instance, claim 24 contains 101 different SEQ ID NOs, along with 5 additional sequences. The various SEQ ID NOs do not appear to contain a common core or other common technical feature. The breakdown of the various sequences is included in the breakdown of the Groups above.

The species listed above do not related to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: As indicated above, the sequences do nor share a common special technical feature so as to unite them under unity of invention.

The inventions listed as Groups I-IX do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the lack the same or corresponding special technical features for the following reasons:

According to PCT Rule 13.2, unity of invention exists only when there is a shared same or corresponding special technical feature among the claimed inventions. Groups I-IV, are directed to hepadnavirus core antigen sequence, but each group has a different technical feature not shared by the remaining groups.

Additionally, according to PCT Rule 13.2, unity of invention exists on when the shared same or corresponding special technical feature is a contribution over the prior art. Whether or not any particular technical feature makes a contribution over the prior art, and therefore constitutes a "special technical feature," is considered with respect to the novelty and inventive step. See, MPEP § 1850.

The inventions listed as Groups I-X do not relate to a single inventive concept because the lack the same or corresponding special technical feature.

The technical feature of Group I, is a non-primate core antigen sequence having a heterologous antigen linked thereto, which is shown by U.S. Pub. No. 2003/0054337 A1 to Birkett (or Pumpens et al., Hepatitis B virus core particles as epitope carriers (1999) Intervirology 38: 63-67) to lack novelty or inventive step as this reference teaches non-primate core antigen sequences (see paragraph [1118] disclosing sequence from woodchuck and ground squirrel hepatitis B virus) having a heterologous antigen (in particular a malaria antigen) linked thereto, and thus Group I does not make a contribution over the prior art. Thus, the technical feature of Group I is not a special technical feature.

The technical feature of Group I, Subgroup I is a non-primate core antigen sequence wherein the sequence is a rodent hepadnavirus core antigen sequence, which is shown by U.S. Pub. No. 2003/0054337 A1 to Birkett to lack novelty or inventive step as this reference teaches non-primate core antigen sequences (see paragraph [1118] disclosing sequence from woodchuck and ground squirrel hepatitis B virus) having a heterologous antigen (in particular a malaria antigen) linked thereto, and thus Group I, Subgroup I does not make a contribution over the prior art. Thus, the technical feature of Group I, Subgroup I is not a special technical feature.

The technical feature of Group I, Subgroup K is a non-primate core antigen sequence wherein the sequence is an avian hepadnavirus core antigen sequence, which is shown by Pumpens et al., Hepatitis B virus core particles as epitope carriers (1999) Intervirology 38: 63-67 to lack novelty or inventive step as this reference suggests the use of avian hepadnaviruses (DHV and HHV) as epitope carriers (see page 64, column 2), and thus Group I, Subgroup K does not make a contribution over the prior art. Thus, the technical feature of Group I, Subgroup K is not a special technical feature.

The technical feature of Group II, is a primate core antigen sequence having a heterologous antigen linked thereto, which is shown by U.S. Patent Number 5,990,085 to Ireland et al. to lack novelty or inventive step as this reference teaches primate core antigen sequences having a heterologous antigen (in particular a inhibin antigen) linked thereto with the C-terminal portion replaced by 1-100 amino acids where those 1-100 amino acids do not consist of cysteine or wild-type C-terminal sequence (see column 7, lines 45-65), and thus Group II does not make a contribution over the prior art. Thus, the technical feature of Group II is not a special technical feature.

The technical feature of Group II, Subgroup I is a primate core antigen sequence where the core antigen sequence is a hepatitis B sequence, which is shown by U.S. Patent Number 5,990,085 to Ireland et al. to lack novelty or inventive step as this reference teaches human core antigen sequences, and thus Group II-I does not make a contribution over the prior art. Thus, the technical feature of Group II-I is not a special technical feature.

The technical feature of Group II, Subgroup P is a primate core antigen sequence where the members of the group are united by the fact that they are "non-human." Referring to these viruses as "non-human" does not create a feature which is technical, but instead is merely a label. As has been evidenced above, primate hepadnaviruses are known. The exclusion of sequences which are human does not create a technical feature within the groups so as to link them while excluding the human sequence. One could argue that a technical feature that links the groups of primate HBVs is that they are all HBVs. Once you exclude "human" HBVs then the technical feature of being HBVs is excluded as well. Thus, there is nothing left to link the group of non-human HBVs. As such, there is no technical feature which unites Group II-P. Thus, the feature common to Group II does not constitute a technical feature over the Group from which it follows that there is no "special technical feature" of the group. Moreover, as is indicated above and in references including Pumpens et al., it is well-known in the art that the core sequences are highly conserved and that other animal/mammalian sequences can be substituted for the human core sequence. Therefore, the substitution of the "non-human" sequence would lack inventive step.

The technical feature of Group III is a non-primate core antigen sequence that comprises a loop region wherein the C-terminal sequence of the core antigen is replaced by 1-100 amino acids, which is shown by U.S. Pub. No. 2003/0054337 A1 to Birkett to lack novelty or inventive step as this reference teaches non-primate core antigen sequences wherein the C-terminal sequence of the core antigen is replaced by 1-100 amino acids (see claim1, part d and paragraph [0118] disclosing sequences from woodchuck and ground squirrel hepatitis B virus), and thus Group III does not make a contribution over the prior art. Thus, the technical feature of Group III is not a special technical feature.

The technical feature of Group V, is methods of making the compounds of Group III. As indicated immediately above, Group III does not make a contribution over the prior art, as U.S. Pub. No. 2003/0054337 A1 to Birkett (or Pumpens et al., Hepatitis B virus core particles as epitope carriers (1999) Intervirology 38: 63-67) shows this group to lack novelty or inventive step as this reference teaches methods of making non-primate core antigen sequences wherein the C-terminal sequence of the core antigen is replaced by 1-100 amino acids (see claim1, part d and paragraph [0118] disclosing sequences from woodchuck and ground squirrel hepatitis B virus), and thus Group V does not make a contribution over the prior art. Thus, the technical feature of Group V is not a special technical feature.

The technical feature of Group V, Subgroup D is a non-primate core antigen sequence wherein the sequence is an avian hepadnavirus core antigen sequence, which is shown by Pumpens et al., Hepatitis B virus core particles as epitope carriers (1999) Intervirology 38: 63-67 to lack novelty or inventive step as this reference suggests the use of avian hepadnaviruses (DHV and HHV) as epitope carriers (see page 64, column 2), and thus Group V, Subgroup D does not make a contribution over the prior art. Thus, the technical feature of Group V, Subgroup D is not a special technical feature.

The technical feature of Group VI is methods of modifying a primate hepadnavirus core antigen that is heterologous to the core antigen and replacing the C-terminal region by the addition of 1-100 amino acids, which is shown by Jegerlehner, A et al., A molecular assembly system that renders antigens of choice highly repetitive for induction of protective B cell responses (2002) Vaccine 20: 3104-3112 to lack novelty or inventive step as this reference teaches such methods (see for instance pg. 3105, column 2, construct ab2) and thus Group VI does not make a contribution over the prior art. Thus, the technical feature of Group VI is not a special technical feature.

The feature of Group Vi, Subgroup D is methods of modifying a primate hepadnavirus core antigen where the members of the group are united by the fact that they are "non-human." Referring to these viruses as "non-human" does not create a feature which is technical, but instead is merely a label. As has been evidenced above, primate hepadnaviruses are known. The exclusion of sequences which are human does not create a technical feature within the groups so as to link them while excluding the human sequence. One could argue that a technical feature that links the groups of primate HBVs is that they are all HBVs. Once you exclude "human" HBVs then the technical feature of being HBVs is excluded as well. Thus, there is nothing left to link the group of non-human HBVs. As such, there is no technical feature which unites Group II-P. Thus, the feature common to Group II does not constitute a technical feature over the Group from which it follows that there is no "special technical feature" of the group. Moreover, as is indicated above and in references including Pumpens et al., it is well-known in the art that the core sequences are highly conserved and that other animal/mammalian sequences can be substituted for the human core sequence. Therefore, the substitution of the "non-human" sequence would lack inventive step.

Group I is directed towards non-primate core antigen sequences, which has the technical feature of being derived from a non-primate and having a heterologous antigen linked thereto. As outlined above, this technical feature does not make a contribution over the prior art. .

Group II is directed towards primate core antigen sequences, which has the technical feature of being derived from a primate and having a heterologous antigen linked thereto. As outlined above, this technical feature does not make a contribution over the prior art.

Group III is directed towards non-primate core antigen sequences, which has the technical feature of being derived from a non-primate and having the C-terminal sequence of the core antigen is replaced by from 1 to 100 amino acids. As outlined above, this technical feature does not make a contribution over the prior art.

Group IV is directed towards primate core antigen sequences, which has the technical feature of being derived from a primate and having the C-terminal sequence of the core antigen is replaced by from 1 to 100 amino acids. As outlined above, this technical feature does not make a contribution over the prior art.

Group V relates to a method of making the compound of Group III. As outlined above, this technical feature does not make a contribution over the prior art.

Group VI relates to a method for modifying primate hepadnavirus core antigen including replacing the C-terminal sequence.

Group VII relates to a method of making a compounds which has the technical feature of being derived from a non-primate and having a heterologous antigen linked thereto, where the linked antigen is further modified.

Group VIII relates to a method of producing an immune response where the technical feature is the administration of a polypeptide, wherein the polypeptides is a non-primate core antigen linked to an antigen and/or administration of the nucleic acid encoding the polypeptide.

Group IX, relates to a method of producing an immune response using a hepadnavirus core antigen wherein the technical feature is a methods of producing an immune response using a primate hepadnavirus core protein linked to a heterologous antigen where the C-terminal sequence of the core antigen is replaced by 1-100 amino acids devoid of Cys or the wt sequence and/or vectors encoding the aforementioned core protein-heterologous antigen polypeptide.

Group X relates to methods for producing an immunogenic composition comprising a primate hepadnavirus core antigen, including modifying the core antigen.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/23391

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-4 and 103-106

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.